

CENTRAL INTELLIGENCE AGENCY		REPORT	STAT
INFORMATION REPORT			
RESTRICTED			
FOR OFFICIAL USE ONLY		DATE DISTR. 31 August 1948	
UNCLASSIFIED		NO. OF PAGES 17	
JAN 31 1955		NO. OF ENCL'S. (LISTED BELOW)	
FOR OFFICIAL USE ONLY		SUPPLEMENT TO REPORT NO.	

THIS DOCUMENT CONTAINS INFORMATION AFFECTING THE NATIONAL DEFENSE OF THE UNITED STATES WITHIN THE MEANING OF THE ESPIONAGE ACT OF 1917, U.S.C. 51 AND 52, AS AMENDED. ITS TRANSMISSION OR THE REVELATION OF ITS CONTENTS TO AN UNAUTHORIZED PERSON IS PROHIBITED BY LAW. REPRODUCTION OF THIS FORM IS PROHIBITED. HOWEVER, INFORMATION CONTAINED HEREIN MAY BE UTILIZED AS NECESSARY BY THE RECEIVING AGENCY.

THIS IS UNEVALUATED INFORMATION FOR THE RESEARCH USE OF TRAINED INTELLIGENCE ANALYSTS

SOURCE Russian periodical, Izvestiya Akademii Nauk SSSR, Otdeleniye Khimicheskikh Nauk, No 3, May/June 1947. FDB Per Abs 15T23 -- Translation specifically requested.)

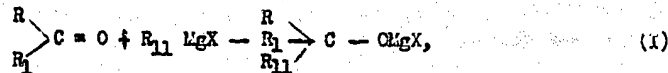
INTERACTION OF GRIGNARD REAGENTS WITH CARBONYL COMPOUNDS

A.D. Petrov and E.P. Kaplan
Inst Org Chem Acad Sci USSR
Submitted 29 April 1946

[Numerals in parentheses refer to the appended bibliography]

On the basis of data in the literature of the subject, as well as newly undertaken experimental research into the interaction of diverse Hg--alkyl halides with various carbonyl compounds, we propose to arrange radicals in the order of decreasing negative charge. The classification of radicals makes it possible to give a detailed account of the mechanism of the Grignard synthesis and to predict the probable course of reactions not yet produced.

In the works devoted to the investigation of the mechanism of the Grignard reaction (we have in mind the works of Hess (1), Leisenheimer (2), Pfeifer and Blank (3), Neamyanov, A. N. Sazonova (4) and others), the reaction mechanism was studied on the basis of a relatively small number of experiments. The discussion in these investigations was centered around the question of the correctness of the schematic Grignard equation,



which provides for the formation of carbinolate 1, as the primary intermediate

- 1 -

CLASSIFICATION		FOR OFFICIAL USE ONLY	
STATE	<input checked="" type="checkbox"/> NAVY	<input checked="" type="checkbox"/> NSRB	DISTRIBUTION
ARMY	<input checked="" type="checkbox"/> AIR	<input checked="" type="checkbox"/> REC	

RESTRICTED

RESTRICTED

STAT

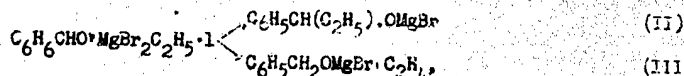
product toward the synthesis of alcohols. After repeating critically the experiments of the German authors and studying in detail the products of addition, the authors of the last-mentioned works (Neameyanov and Sazonova) rejected the idea of the primary formation of complex additions, giving preference to the original Grignard system of the equation (I') type:



By way of supplementing these investigations, we are attempting to approach the Grignard mechanism of alcohol synthesis not by studying the structure of the complexes, but from a somewhat different point of view.

The aim of the present study is a critical comparison of the reaction materials -- diverse ketones with various alkyl halides -- to determine the peculiar features of various reactions and general laws which would make it possible to predict the course of the reaction even in syntheses not yet produced.

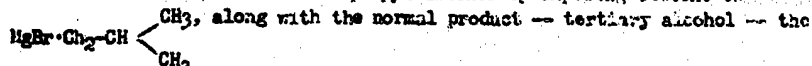
First, it is necessary to point out that Meisenheimer's idea of the original formation of a complex addition which is either isomerized into carbinolates (II) or decomposes with the formation of olefins



is not correct in its first part. But Meisenheimer's work is valuable if only because it raises the question of the desirability of supplementing the Grignard equation and giving it a greater flexibility in order that it may better embrace a great diversity of factual data.

Furthermore, Meisenheimer's work emphasizes the facts that an ether medium, low temperatures, and an excess of Mg-alkyl halides favor a reaction in accordance with equation II. On the other hand, increases in temperature and an excess of a carbonyl compound are favorable to reduction reactions, i.e., processes occurring in accordance with equation III. Knowledge of these facts permits a certain amount of control over the reaction, even though that control is within very narrow limits.

It should be borne in mind that Meisenheimer studied the mechanism of Grignard's synthesis exclusively on the basis of carbonyl compounds incapable of enolization (benzole, cinnamic, and croton aldehydes). Of those compounds which are capable of enolization he touched lightly upon only two. He exposed acetone to the action of MgBr-ethyl, and after 3 hours of boiling in benzene (elimination of ether) he was unable to get isopropyl alcohol. Yet it is known that Sabatier and Mailhe (5), even under normal conditions of temperature and in an ether medium, obtained isopropyl alcohol by exposing acetone to



formation of which was also recorded in the work of M. K. Konovalov (6). Again, in the action of propionic aldehyde upon Mg-bromophenyl, after long boiling in

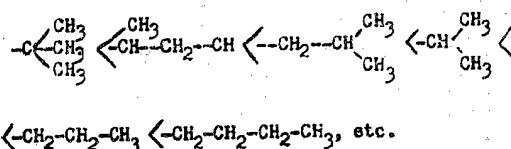
RESTRICTED

STAT

benzene, Meisenheimer obtained only phenylethylcarbinol, without any trace of benzyl alcohol. (It is known, however, that when benzaldehyde is acted upon by Mg-bromoethyl, benzyl alcohol is obtained in considerable quantities.)

These examples confirmed the fact that the products of reduction are frequently formed not in the process of decomposition of carbinols but as a result of the decomposition of the Mg-alkyl halides in accordance with equation III.

It developed that the alkyl halides which are capable of decomposition are the less stable the more ramified their structure, and the closer their side chains are to carbon which is connected with the halide molecule. The alkyl halides can be arranged in the following series showing the order of increasing stability of their radicals:



(However, the relative stability of these radicals (examples will be given below) is fully determined by the nature of the radicals of the carbon compounds, with which they have to interact.)

The radicals of the secondary and tertiary alkyl halides (and the n-propyl and isobutyl of the primary) have often proved themselves particularly unstable, and have either tended toward the formation of olefins (R-H) and cupellation [sic] (R-R) or in the direction of disproportion (7,8,9,10) (R+R+R-R).

Not long ago Kharasch (11) showed that benzophenone and isophorone, which under normal conditions react with CH_3MgBr in the direction of tertiary alcohols, produce pinacols when added to the Grignard reagent CoCl_2 , which apparently facilitates the dissociation of the reagent and the formation of ethane.

We, too, were able, under the conditions followed by Kharasch, to obtain pinacols from a substance similar to isophorone-3-5 (dimethylcyclohexene)-2-one-1, but were unable to obtain pinacols from acetophenone. Apparently pinacols are formed only from those ketones which are activated by the presence of multiple bonds and which, at the same time, are either incapable of enolization or are little inclined to it.

The formation of reduction products of secondary alcohols and pinacols, as a phenomenon depending on the structure of the alkyl halides and ketones, has been commented upon by investigators from the very beginning of their studies of the Grignard reaction. M. I. Konovalov was among the first to point this out.

Blick and Powers (13) recently pointed out that the action of $\text{CH}_3\text{CH}_2\text{CH}_2\text{MgBr}$ upon phenyl- α -naphthyl ketone forms a product of reduction corresponding to secondary alcohol with a yield of 65%. The action of the same

RESTRICTED

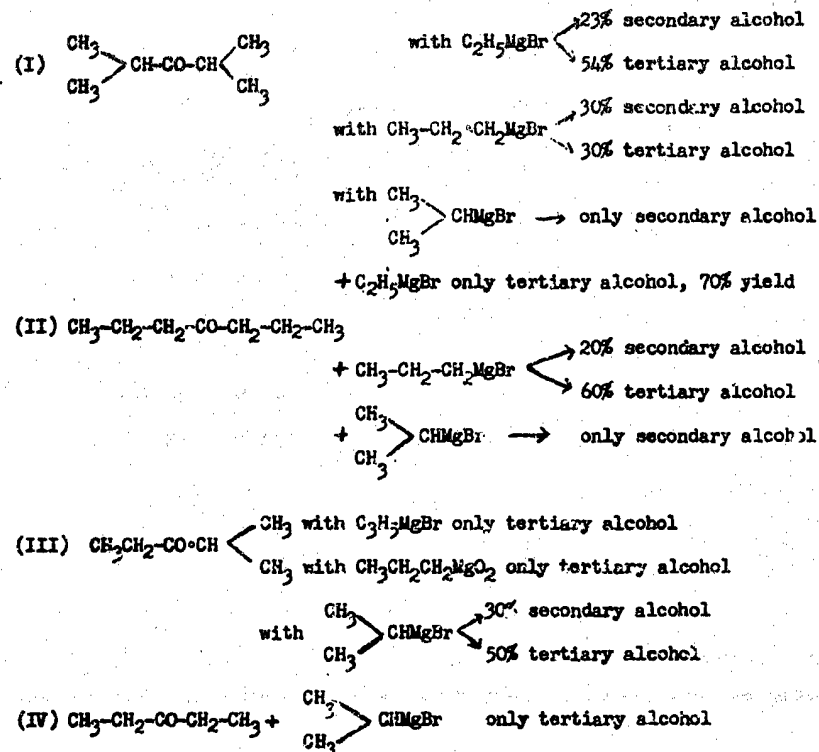
STAT

alkyl halide upon phenyl benzyl ketone forms a product of reduction with a yield of only 9%; the principal product proved to be tertiary alcohol. During the action of $n\text{-CH}_3\text{-CH}_2\text{-CH}_2\text{-CH}_2\text{MgBr}$ upon benzophenone, as shown by Crawford (14), only benzohydrol is formed; while the action of the same alkyl halide upon acetone forms only dimethylbutylcarbinol (15). The action of $\text{Mg-chlorocyclohexyl}$ upon acetone (16) and acetophenone (17) forms corresponding tertiary alcohols, while the action of the same alkyl halide upon dicyclohexyl ketone forms only dicyclohexylcarbinol (18).

Acetaldehyde in combination with MgBrC_2H_5 produces secondary butyl alcohol (19) and chloral-trichlorethyl alcohol (20).

MgI-propyl with acetophenone (21) and pinacolin produces tertiary alcohols; with trimethylacetophenone it produces secondary alcohol and tertiary-butylphenylcarbinol (22).

Stas (23) showed that under action of various Mg-alkyl halides , diisopropyl ketone, butyrons, and ethylisopropyl ketone produce various yields of secondary and tertiary alcohols:



STAT

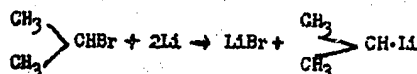
These observations may be supplemented by experiments made on the action of tertiary Mg-bromobutyl on acetone, methylpropyl ketone, and pinacolin (24). Whereas the first ketone gives a good yield of tertiary alcohol, in the case of the second ketone the yield of tertiary alcohol drops to 50% and pinacolin forms only condensation products. We thus see that the hindrances encountered in the interaction between ramified Mg-alkyl halides (isopropyl, tertiary butyl) and ketones increase with the increase in molecular weight and the degree of replacement of the ketones (in other words, with the increase of steric hindrances). It should also be noted that whereas the synthesis of methyl-tert-butylcarbinol cannot be effected through the action of Mg-chloro-tert-butyl pinacolin, that alcohol is easily obtained as a result of lengthy interaction of hexamethylacetone with CH_3MgI (25) (not disposed toward the breaking-up of radicals).

Of considerable interest are the data obtained by Noller (26) in his experiments on the synthesis of benzophenone by means of various Grignard reagents.

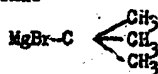
Apparently, the course of the reaction of the Grignard synthesis of alcohols (the trend toward alcohols, products of reduction, or the condensation of ketones) is frequently determined by the so-called steric hindrances, which depend on the emerging arrangement of radicals, as well as on the way in which the arrangement is formed. We underline especially the importance of the way in which a particular configuration is formed.

By way of supplementing the previously cited examples of reactions studied by Stas, it is necessary to point out that triisopropylcarbinol, for instance, cannot be obtained by the Grignard synthesis only. But the form of this alcohol is sufficiently stable and is capable of existing, a fact which has been recently proved by the synthesis of the alcohol through the action of isopropylbromide on diisopropyl ketone in the presence of lithium (27).

It is possible that in the latter case the reaction takes place initially in accordance with the scheme



and that subsequently the lithium organic compound reacts with the ketone. It is also interesting to observe that



which decomposes easily under high temperatures (in which case it functions as a reducing agent), as well as by interaction with sterically hindered ketones already containing tertiary radicals within their molecules, reacts quantitatively in an ether medium with benzophenone, forming diphenyl-tert-butylcarbinol.

It is clear from the examples above that carbonyl compounds incapable of enolization (benzophenone, hexamethylacetone, chloral, etc.), as well as those

~~RESTRICTED~~

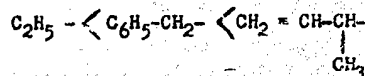
STAT

capable of enolization but not sufficiently enolized on account of the peculiarities of their structure (pentamethylacetone, diisopropyl ketone), stimulate the breakup of the Grignard reagents into radicals (and the latter into olefins and hydrogen) by virtue of the fact that they are acceptors of hydrogen. However, among the ketones which are capable of enolization there are those with structures distinguished by opposite properties, namely, the capacity under specific conditions, or under the influence of certain alkyl halides, to undergo enol conversions and to function not as an acceptor but as a donor of hydrogen. Fr. Whitmore (28) cites instances of interaction with some of the ketones belonging to this group.

Enolization is especially great when quaternary carbon associated with three ethyl radicals is present alongside the carbonyl group. However, when the side chains find themselves in β -position with respect to carbonyl, enolization drops to zero. The enolization percentage of ketones is not only subject to change under the influence of a single alkyl halide, parallel to changes in the ketone structure, but in the case of a single ketone the percentage of enolization may change in connection with the transition from one alkyl halide to another.

While the action of C_2H_5MgBr on acetomesitylene resulted only in the product of enolization (29), with a yield of 100%, the action of $C_6H_5-CH_2-MgBr$ on the same ketone yielded 38% of the product of enolization and the normal addition compound -- the corresponding tertiary alcohol -- at 52% (30). Finally, when the same ketone was acted upon by β -butenylbromide $CH_2=CH-CH_2-Br$, tertiary alcohol was obtained with a yield of 83%.

It will be seen, therefore, that parallel with the growth in the stability of radicals, as affecting the breakup and the splitting off of hydrogen (and also, apparently, its addition),



there is a drop in the percentage of enolization of a ketone (i.e., the equilibrium condition of the latter shifts toward the ketone form under the influence, as it were, of the gradual stepwise increase in acidity of the medium). Aldehydes which are capable of enolization and symmetrical ketones with a normal or isostructure (but with side chains in β -position or further in relation to carbonyl), show no tendency either to become acceptors of hydrogen (as in compounds incapable of enolization), or to be donors of hydrogen (as is the case of asymmetrical compounds capable of enolization, which have been mentioned above). Therefore, these compounds form normal products of synthesis (secondary or tertiary alcohols) with almost every possible radical.

The above-mentioned limitations in the method of constructing alcohols of the desired structural types may be overcome not only by changing the course of synthesis (examples of which have been cited above), but also by the introduction of multiple bonds either in the alkyl halide or in the carbinol compound.

While propyl, as well as the higher, normal and saturated alkyl halides produce with benzophenone, only benzohydrol, the action of Mg -bromo allyl on both benzophenone (31) and tolylphenyl ketone (32), produces tertiary alcohols with an excellent yield (up to 90%).

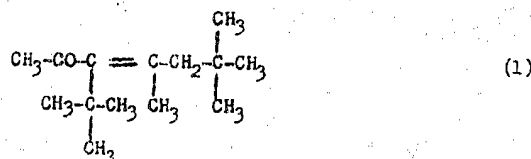
~~RESTRICTED~~

DECLASSIFIED

STAT

An excellent yield of tertiary alcohol is also obtainable when $MgBr$ -heptenyl acts upon benzophenone (33). An analogous effect is produced by introducing a multiple bond into carbonyl compounds. We have already noted that the yields of tertiary alcohols which are formed as a result of the action of Mg -bromo-tert-butyl upon ketones drop sharply with the transition from acetone to the higher molecular ketones and especially the branching ketones. However, as has recently been shown by A.D. Petrov, V.I. Koptev, and E.P. Kaplan, Mg -bromo-tert-butyl, when reacting with mesityl oxide, produces good yields of tertiary alcohol (50%) if the reaction is conducted at low temperatures.

Likewise, tertiary alcohol, as the present investigation has shown, is obtained as a result of the action of H - Mg -bromooctyl upon 3-tert-butyl-6,6-dimethylheptene-3-one-2. This ketone (1), which we synthesized for the first time (by the action of acetic anhydride upon triisobutylene) in the apparatus of Tserevitinov,



reacted as alcohol (enol) with CH_3MgI yielding only 12%, with n - Mg -bromooctyl the ketone yielded 33%, producing the normal product of reaction, tertiary alcohol of the $\text{C}_{22}\text{H}_{44}\text{O}$ composition with a yield of 29%, and the product of reduction, secondary alcohol of the $\text{C}_{14}\text{H}_{28}\text{O}$ composition.

The foregoing brief survey shows the many-sided character of the Grignard synthesis of alcohols and the impossibility of remaining satisfied with the old scheme (equations I, II, III), since that scheme does not account sufficiently for the changes in the course of the synthesis produced by the changes in the structure of the components, even when the synthesis takes place under normal conditions (at low temperatures and in an ether medium).

In the case of analogues of Mg -organic compounds and Na -organic compounds, considered as salts, Morton (35) recently gave a close quantitative evaluation of the "acidity" of individual radicals, in part, very likely appearing as anions.

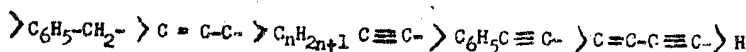
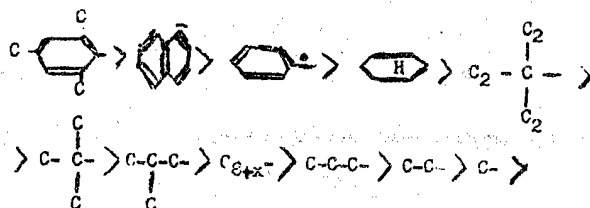
If we limit ourselves to the qualitative evaluation of the relative "acidity" of radicals participating in the Grignard synthesis, we believe that the material assembled enables us to make a more detailed evaluation of the acidity (negative charge) of individual radicals, as well as to supplement the basic equations of the Grignard synthesis with the following observations:

1. Radicals of organic compounds may be arranged in the order of decreasing affinity capacity (to employ the older terminology), or in

~~RESTRICTED~~

STAT

accordance with their increasing acidity (diminishing negative charge), if we use the newer terminology



In surveying the course of alcohol syntheses it is necessary to take into consideration the charges of radicals of carbonyl compounds and of Grignard reagents, as well as the steric hindrances associated with these radicals.

If, for instance, in the original ketone R-CO-R the two radicals are mesityls, i.e., are characterized by an increasing affinity capacity (negative charge) and the greatest steric hindrances, then to the "weakened" bond of the central carbon only hydrogen can be added. (This can be expressed in different terms, as follows: two highly negative charges make possible the addition of the positively charged hydrogen).

R-naphthyl or phenyl, which are characterized by high negative charges and relatively small steric hindrances, are readily united with alkynes, alkenes, and elements which are incapable of breaking-up with the formation of olefins -- naphthyl, phenyl, and methyl. (In this case the middle members of the series of the alkyl halide radicals break up, i.e., the reaction proceeds in accordance with equation III, which is facilitated by the tendency of the nonenolizable ketones to be acceptors of hydrogen).

If, on the other hand, hydrogen atoms (formaldehydes) are associated with the carbonyl group, that is, if the central carbon possesses a high positive charge, it is obviously able to function easily as an acceptor of any negatively charged radical. We know, in fact, that all Mg-alkyl halides react with formaldehyde, and that $\text{C}_6\text{H}_5\text{---CH}_2\text{---}$ is even isomerized in $\text{CH}_3\text{---C}_6\text{H}_5$, which results in the increase of the radical's negative charge, i.e., a complete equalization of charges is made possible.

2. If in the original ketones (aldehydes) the radicals are related to the middle members of the series -- ethyl-octyl or isoalkyl -- but have a side chain sufficiently removed from carbon which is associated with carbonyl, such carbonyl compounds, whose radicals are of medium negative charge, are characterized by the fact that the bond leading to the alkyl halide is of normal stability. In this instance, therefore, alcohol is obtainable with almost every radical of the series, i.e., the reaction proceeds mainly in accordance with equation II (which is also facilitated by the small steric hindrances characteristic of this group of radicals).

~~RESTRICTED~~

STAT

3. In the case of asymmetrical ketones which have one enolizable radical of medium negative charge and another radical of high or low negative charge and a sterically hindered structure, the ketone becomes more or less enolized and turns into a "donor of hydrogen" if it interacts with the middle members of the series of radicals capable of being hydrogen acceptors.

In conclusion let us note that Kharash and Weinhouse (36) earlier advanced the idea that there is a dependence relationship between the negative charge of the radical of the Grignard reagent and its capacity to unite with a carbonyl compound or to reduce it. These authors, in studying the interaction of benzophenone with various alkyl halides, have arranged the latter into a series in the order of the decreasing negative charge of their radicals.

We share these ideas and we treated them in somewhat greater detail, endeavoring to show the influence exercised on the course of the Grignard synthesis by the magnitude of the charge of alkyl halide radicals as the radicals composing carbonyl compounds. In distributing the radicals into a series we endeavored also to take into account the steric hindrances of certain of these radicals (which, for example, explains the place assigned to the tertiary butyl radical in our series). Finally, we made a supplementary study of the possibility of reduction, in the case of certain structures of carbonyl compounds, not of the compounds themselves, but of the Grignard reagents; and we have shown that for the suppression of both of these reduction reactions it is important to introduce multiple bonds into the carbonyl compounds or into the alkyl halides (thereby conditioning the "activation" of the normal reaction, or the reaction of addition). The series of radicals cited above enabled us to predict the course of the Grignard synthesis for reactions not yet produced. The correctness of the prediction has been verified experimentally.

Experimental Results

1. Interaction of H-Mg-bromooctyl with 3-tert-butyl-6, 6-dimethylheptene-3-one-2.

(By E. P. Kaplan)

The ketone was synthesized in accordance with the general method of ketone synthesis from olefins of hydrocarbons and acetic anhydride in the presence of $ZnCl_2$, recently refined by Berms and Doravani (37). The ketone thus obtained, apparently for the first time, at a yield of 33%, is a fluid with an agreeable odor and a boiling point of 226-228°.

d_4^{20} 0.8627; n_D^{20} 1.4561

MR found, 66.22; MR calculated, 66.39

M found, 210.2; M calculated, 210

Analysis: Found - C, 80.43%; H, 12.18%

Calculated for $C_{14}H_{26}O$ - C, 80.17%; H, 12.38%

STAT

~~RESTRICTED~~

The ketone yields a semicarbazone with a melting point of 158° . M_n $\sqrt{[c]_D^{20}}$, 2.730; t_D^{20} , 18; p_D , 752.1; V , 0.358; N , 15.245. Calculated for $C_{15}H_{28}O$: N , 15.7%. The bromine number of the ketone, defined in accordance with Kaufmann, is 103; calculated, 76. The increased bromine number we attribute to the enolization of the ketone. The ketone was subjected to ozonization. Among the products of ozonization it was possible to identify only a ketone with the melting point of semicarbazone, 172° , corresponding to the semicarbazone of methylneopentyl ketone.

Furthermore, considering the fact that according to Whitmore and Wilson (38) 90% of triisobutylene consists of 2,2,4,6,6-pentamethylheptene-3 and 2, 2-dimethyl-4-neopentylpentene-4 (this form differs from the preceding one only by the position of the multiple bond), we conclude that the synthesized ketone is primarily 3-tert-butyl-6,6-dimethyl-heptene-3-one-2.

In order to obtain the Grignard reagent we took 5 gr kg, 40 gr octylbromide and 150 cc of ether. To the reagent at 3 to 5° was then added in the course of 5 hours 28 gr of the ketone dissolved in 50 cc of ether. Stirring was continued for several hours, first at room temperature, then at the boiling point of ether. Upon the dissolution of the complex by frequent fractionation of the product of reaction, the following fractions were separated:

Fraction I, 115-122 $^{\circ}$, 6 gr; fraction II, 192-195 $^{\circ}$, 9 gr; fraction III, 169-172 $^{\circ}$ at 8 mm, 11 gr.

Fraction I proved to be 1-octene; d_4^{20} 0.7153; n_D^{20} 1.4082. The bromine number, by Kaufmann's method, is 139. The calculated bromine number is 143; M found, 110; M calculated, 112.

Fraction II had the following properties: d_4^{20} 0.8344; n_D^{20} 1.4395; M found, 210; M calculated for $C_{14}H_{28}O$, 212; MR found, 66.8; MR calculated, 67.49.

Analysis: Found - C, 80.77%; H, 12.13%
Calculated for $C_{14}H_{28}O$ - C, 79.2%; H, 12.7%

Definition of the number of hydroxyl groups by the Chugayev-Tseretnikov method: found, 8.0%; calculated for $C_{14}H_{28}O$, 7.99%

Fraction III, d_4^{20} 0.8450; n_D^{20} 1.4604; M found, 327; M calculated, 324, MR found, 105; MR calculated, 105.5.

Analysis: Found - C, 81.97%; H, 13.17%
Calculated for $C_{22}H_{44}O$ - C, 81.48%; H, 13.58%

Definition of the number of hydroxyl groups by the Chugayev-Tseretnikov method: found, 5.2%; calculated for $C_{22}H_{44}O$, 5.2%

Thus, the second fraction proved to be secondary alcohol, the reduction product of the ketone, while the third fraction proved to be tertiary alcohol.

~~RESTRICTED~~

STAT

2. Interaction of Methyl-Mg-Bromide with 3,5-Dimethylcyclohexene-2-one in the Presence of CoCl_2

(By E. P. Kaplan)

For this reaction experiment we took 3 gr of Mg shavings and 30 cc of ether, through which a stream of CH_3Br was conducted at room temperature. In an hour the reaction began, and the preparation of the Grignard reagent proceeded with the ether boiling gently. Upon the disappearance of the Mg shavings, the Grignard solution was decanted and 0.3g CoCl_2 added to it. While CoCl_2 was being added, the temperature was raised from 15 to 33°. Half an hour later there was added 12 gr of 3,5-dimethylcyclohexene-2-one-1 with a boiling point of 208-210°, n_D^{20} 1.4900 dissolved in 20 cc of ether at a temperature of 10 to 12°. After all of the ketone had been added, the stirring process continued for 3 to 4 hours at the boiling point of ether, and the mixture was left standing overnight. It was broken down by small pieces of ice with CH_3COOH ; upon fractionation there were obtained: Fraction I, 180-185°, 6 gr; fraction II, residue in the form of resinous mass, 5 gr.

Fraction I had the following constants:

n_D^{20} 1.4550; d_4^{20} 0.9016

Semicarbazone with a melting point of 178°

Fraction II after 2 days became crystallized. By means of recrystallization from the alcohol, 4 gr of crystals were obtained with a melting point of 166°. The molecular weight in benzene, by the cryoscopic method, is 0.2684 gr mass; 17.06 gr of benzene Δt 0.325°, M found, 246; M calculated for $\text{C}_{16}\text{H}_{26}\text{O}_2$, 250.

Microanalysis:

4.678 mg mass; 4.345 mg H_2O ; 13.106 mg CO_2
3.032 mg mass; 2.885 mg H_2O ; 8.500 mg CO_2

Fraction I, found - H, 10.38%; C, 76.41%
Fraction II, found - H, 10.46%; C, 76.46%

Calculated for $\text{C}_{16}\text{H}_{26}\text{O}_2$ - H, 10.4%; C, 76.8%

Definition of the hydroxyl groups by the Chugayev-Tseretitinov

method:

0.1454 gr mass; 27.4 cc CH_4 (20°, 759 mm)
Found - OH, 13.3%
Calculated for $\text{C}_{16}\text{H}_{26}\text{O}_2$ - OH, 13.2%

Fraction II can thus be seen to be pinacol 3,5-dimethylcyclohexene-2-one-1. Fraction I, insofar as it produces semicarbazone with a melting point of 178° (the melting point of semicarbazone 3,5-dimethylcyclohexene-2-one-1), is in part, no doubt, the initial ketone. But since fraction I boils at a point below that of the initial ketone (about 200°) and possesses a lower refraction, it is apparent that the fraction also contains the hydride of the initial ketone.

STAT

Synthesis With Acetophenone

For this reaction we took 5 gr Mg shavings and 50 cc of ether, through which a stream of CH_3Br was conducted. 0.5g COCl_2 was added at a temperature of 10-15° and 20 gr of acetophenone was added at the same temperature. All conditions were the same as in the preceding synthesis.

Upon fractionation there were obtained

- I. 190-203°, 3 gr
- II. 215-220° (at 15 mm, 89°), 15 gr

Fraction II had the following properties:

n_D^{20} 1.5325; d_4^{20} 0.9735

Definition of the hydroxyl groups by the Chugayev-Tseretintov method:

2155 gr pass; 37 cc CH_4 (18°, 756 mm)
 Found " OH, 12.1%
 Calculated for $\text{C}_9\text{H}_{12}\text{O}$ " OH, 12.5%

Thus, the fraction proved to be dimethylphenylcarbinol.

3. Interaction Between n-Mg-Bromooctyl and Isovaleraldehyde (Between Mg-Bromoisobutyl and n-Butyraldehyde)

(By T. V. Mikhelyan)

Isobutyloctylcarbinol

For this reaction, which was conducted under ordinary conditions in an ether medium, we took: Mg, 11.5 gr; $\text{BrC}_8\text{H}_{17}$, 89 gr; $(\text{CH}_3)_2\text{CH}-\text{CH}_2-\text{C}(=\text{O})\text{H}$, 28 gr (30% less than the theoretical). The entire product of the reaction, which was distilled at 17 mm and in a temperature range of 50-218°, amounted to 64.3 gr. By fractionation the following were separated:

a. A fraction with a boiling point 117-119°, d_4^{20} 0.7232; n_D^{15} 1.411; upon oxidation enanthic acid was separated by means of silver salt.

b. A fraction with a boiling point 126-129°; percentage of hydroxyl groups by Tseretintov's method, 19.12; computed for $\text{C}_{11}\text{H}_{22}\text{O}$, 19.32. In combination with acetyl chloride a product was formed with a boiling point of 136-137° and the characteristic odor of acetic isobutyl ether.

c. From a fraction which had a boiling point of 88-98° there was separated, by means of semicarbazone, pure isovaleraldehyde with a boiling point of 92°, which apparently did not enter into the reaction.

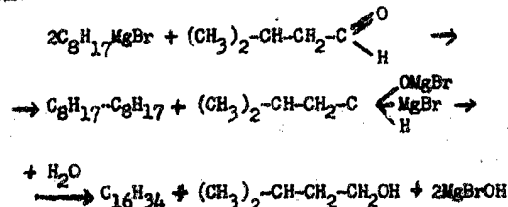
d. From a fraction which had a boiling point of 200° (21 mm) there was separated, by means of fregging and recrystallization, a solid product with a melting point of 20°, d_4^{20} 0.7716. By these constants and the data of elementary analysis the product was identified as hexadecane.

RESTRICTED

STAT

We did not succeed in isolating pure secondary alcohol of isobutyl-octylcarbinol because of its low yield and the presence within the mixture of isoamyl ether of isovaleric acid whose boiling point is close to that of the alcohol.

Thus, in this reaction, reduction processes predominate, proceeding partly in accordance with equation III and in the direction of isoamyl alcohol and octylene, and partly, apparently, in accordance with a somewhat modified scheme



Isobutylpropylcarbinol

For this reaction, which was also conducted under ordinary conditions in an ether medium, we took 25 gr Mg, 142.7 gr $(CH_3)_2CH-CH_2Br$, and 48 gr

$CH_3-CH_2-CH_2-C \begin{array}{c} O \\ \parallel \\ H \end{array}$ (32% less than the theoretical in order to suppress the reduction reactions).

Abundant formation of gas (isobutylene) was noted. The fluid product of reaction amounted to 52 gr. Fractionation produced: fraction I, with a boiling point of 95-140° at 765 mm, 26.9 gr (51.7%); fraction II, with a boiling point of 140-170° at 760 mm, 16.6 gr (32%). Out of the first fraction a small subfraction was extracted with a boiling point of 114-119°, from which, by means of acetyl chloride, butyl acetate with a boiling point of 118-122° was extracted. Propylisobutylcarbinol has already been previously extracted by Mieset (39) by means of $H=C_2H_5MgBr$ acting upon isovaleric aldehyde, and the boiling point of the alcohol, according to this author, was 160-164°. From our fraction with the boiling point of 140-170° we succeeded with the aid of phthalic anhydride, in extracting this alcohol in the form of acid phthalic ether. The ether was saponified with a KOH solution, and the oily film decolated with potash and distilled at a temperature of 159-162°.

The percentage of hydroxyl groups in this fraction, by Tseretininov's method, was 12.35.

The percentage of hydroxyl groups calculated for $C_8H_{17}OH$ was 13.08.

It is clear that in this experiment as well as in the preceding one, reduction reactions dominated the normal course of the process.

Results analogous to our own were obtained by Young and Roberts (40) in the experiment of interaction of secondary- Hg -bromobutyl with isobutyric aldehyde. In this case, too, a large number of butenes were separated.

~~RESTRICTED~~

STAT

22% of the isobutyric aldehyde failed to enter into the reaction; 37% of the product of reaction consisted of isobutyl alcohol; and only 30% consisted of secondary alcohol-isopropyl-secbutylcarbinol.

4. Interaction of $n\text{-MgBrC}_4\text{H}_9$ and Cinnamic Aldehyde, and Benzophenone and MgBrC_2H_5 , MgIC_2H_5 , and $\text{MgBrCH} \begin{smallmatrix} \text{CH}_3 \\ \text{CH}_3 \end{smallmatrix}$

(By Kh. N. Radzhabova and S. M. Polonetskaya)

In the reactions described in section 1, it was expected that the synthesis of tertiary alcohols would predominate while in the reactions treated in section II reduction processes would be preponderant. In producing the above reactions in a benzene medium we expected to obtain reduction reactions only. The experiment confirmed our assumption.

Cinnamic Aldehyde and $n\text{-MgBrC}_4\text{H}_9$

Meisenheimer has already shown that the interaction of cinnamic aldehyde with $\text{MgBrCH}_2\text{-CH} \begin{smallmatrix} \text{CH}_3 \\ \text{CH}_3 \end{smallmatrix}$ in ether produces a secondary alcohol (cinnamylisobutylcarbinol), while the interaction in benzene results only in cinnamic alcohol. We have established that the same results are obtained in the not yet produced reaction between cinnamic aldehyde and $n\text{-MgBrC}_4\text{H}_9$. By adding cinnamic aldehyde to $n\text{-MgBrC}_4\text{H}_9$ in a medium of slightly boiling ether we noticed a peculiar egg-yellow coloring.

For this reaction we took 12 gr Mg, 67 gr $\text{C}_4\text{H}_9\text{Br}$, and 32 gr of cinnamic aldehyde. Upon the disintegration of the complex, 22 gr of the products of the reaction were distilled out; of these 5 gr became crystallized in the form of small needles with a melting point of 33° (after being recrystallized from benzene), making it possible to identify this fraction as cinnamic alcohol.

The remaining 17 gr consisted of a fluid with a boiling point of $149\text{--}150^\circ$, at 20 mm with specific gravity d_{40}^{20} 0.982; n_D^{20} 1.564. M found, 195; M calculated for $\text{C}_{13}\text{H}_{18}\text{O}$, 190 hydroxyl groups by the Chugayev-Tsarevskii method: Found, 10.06; calculated, 8.9.

The experiment was repeated, with the deviation, however, that the cinnamic aldehyde was added drop by drop and the reagent was subjected to considerable freezing. In this case the only product of reaction was a secondary alcohol, butylcinnamylcarbinol.

Action of Benzophenone Upon MgBrC_2H_5 and MgIC_2H_5

An Mg-organic compound was formed by 5.2 gr of Mg and 23.9 gr of $\text{C}_2\text{H}_5\text{Br}$ in a benzene medium. To the reagent, which was heated in a water bath, was added a benzene solution of 40 gr of benzophenone. On the following day the product of reaction was broken down, as usual, and distilled in a vacuum of 15 mm at $175\text{--}185^\circ$. Altogether, 30 gr of the product was distilled, which after recrystallization from ligroin had a melting point of 69° .

~~RESTRICTED~~

~~RECEIVED~~

STAT

M found (after Rast), 181.4; calculated for $C_{13}H_{12}O$, 184.

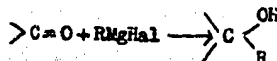
Percentage of hydroxyl groups after Tserevitinov: found, 8.01; calculated for $C_{13}H_{12}O$, 9.4.

Identical benzohydrol with the same yield was obtained as a result of interaction of benzophenone with $MgIC_2H_5$ (in an ether medium these reagents form with benzophenone tertiary alcohol).

Action of Benzophenone upon $MgBrCH(CH_3)_2$

An Mg-organic compound was obtained from 9.2 gr of Mg and 28.7 gr of isopropylbromide, also in a benzene medium. A benzene solution of 70 gr of benzophenone was added to the reagent while it was heated in a water bath. When the product of this reaction was broken down, practically the entire amount of benzophenone, which did not enter the reaction, was separated, with a melting point of 49° . Benzohydrol could not be separated. Isopropylbenzene ($d_{20} 0.857$ and $n_D^{20} 1.472$) was obtained in the amount of 14 gr. Upon repeating the reaction we took 3.5 gr of Mg, 16.2 gr of isopropylbromide + 1% (0.162 gr) CuI, and 24 gr of benzophenone. We separated from the product of reaction: (1) 15 gr (62.5%) benzophenone-benzohydrol; (2) 4 gr (16.6%) benzophenone.

CuI is known as an agent which increases the yields of tertiary alcohols, in accordance with the reaction



Its stimulating action upon reduction reactions proceeding in accordance with equation III is apparently noted for the first time. It is

also interesting to observe that in an ether medium $MgBrCH(CH_3)_2$ is dis-

tinguished by greater stability than, for instance, $MgBrCH_2CH(CH_3)_2$, since under these conditions it produces with benzophenone only 22% of benzohydrol, as has been shown by Blick and Powers (13). On the other hand, in order to reduce benzophenone $MgBrCH(CH_3)_2$ in a hydrocarbon medium it is apparently necessary to have either a higher temperature than one that makes possible boiling in benzene, or the stimulating influence of the addition of CuI.

Conclusions

1. We analyzed the reactions between various carbonyl compounds, and diverse Grignard reagents on the basis of data known in the literature of the subject. We proposed an arrangement of the radicals of carbonyl compounds,

STAT

as well as of the Grignard reagents, into an order of decreasing affinity capacity (decreasing negative charge), which permits anticipation of the course of synthesis even in reactions which hitherto have not been produced.

2. For the first time we performed reactions between:

- a. n-MgBr-octyl and 3-tert-butyl-6,6-dimethylheptene-3-one-2
- b. $\text{CH}_3\text{MgBr} + \text{CoCl}_2$ and (a) 3,5-dimethylcyclohexene-2-one-1 and (b) acetophenone in ether medium
- c. MgBr-isobutyl and n-butyraldehyde
- d. n-MgBr-octyl and isovaleraldehyde
- e. n-Mg-bromobutyl and cinnamaldehyde (in ether and at increased temperature in benzene)
- f. MgBrC_2H_5 and $\text{MgBrCH} \begin{smallmatrix} \text{CH}_3 \\ \text{CH}_3 \end{smallmatrix} + \text{CuI}$ and benzophenone in benzene.

In all these cases the experiments confirm the predicted course of the reaction implied in the analysis of previously performed reactions.

The mechanism of formation and decomposition of carbinolates of various R_2 and R_{II} has been studied; the presence of multiple bonds in carbonyl compounds or in Mg-alkyl halides has been shown to be of a positive influence upon the yield of the desired structural forms of alcohols.

BIBLIOGRAPHY

1. K. Hess and H. Reinboldt, Ber., 54, 2013 (1921); K. Hess and W. Wustow, Ann., 437, 256 (1924)
2. J. Meisenheimer, Ber., 54, 1655 (1921), Ann. 442, 180 (1925)
3. Pfeifer and Blanc, J. prakt. Chem., 153, 242 (1959)
4. A.N. Nesmeyanov and V.N. Sazonova, Izv. AN SSSR, Khim., 4-5 (1941)
5. Sabatier and Mailhe, C.R., 141, 298 (1905)
6. M. J. Kononov, ZhKhO, 37, 349 (1905)
7. G. L. Stadnikov, Anomalies of the Grignard Reaction, Thesis (1916)
8. A. D. Petrov, Izv. AN SSSR, Chemical Series (1938), 2, 347-360
9. A. D. Petrov, K. N. Karasov, M. A. Chel'tsova, ZhKhO, 6, 552 (1937)
- A. D. Petrov, D. N. Andreyev, ZhKhO, 7, 570 (1937); A. D. Petrov, E. B. Sokolova, ZhKhO, 8, 199 (1938); A. D. Petrov, S. S. Sanin, ZhKhO, 8, 195 (1938); 9, 2129 (1939); A. E. Arbuzov and I. A. Arbuzova, ZhKhO, 2, 388 (1932)
10. Bachukan, J. Am. Chem. Soc., 53, 2758 (1931)
11. Tharassch, J. Am. Chem. Soc., 63, 2305, 2308, 2315, 2316, (1941)
12. M. I. Kononov, ZhKhO, 38, 447 (1906)
13. Blick and Powers, J. Am. Chem. Soc., 51, 3378 (1929)
14. Crawford, J. Am. Chem. Soc., 64, 2864 (1942)
15. Edgar, J. Am. Chem. Soc., 51, 1483 (1929)
16. Acres, Ber. 37, 2753 (1904)
17. Sabatier and Mailhe, C.R., 139, 343 (1904)

~~REDACTED~~

STAT

~~REDACTED~~

18. Sebatier and Mailhe, C.R., 141, 298 (1905)
19. Wood, Scary, J. Gas and Oil, 42, 13 (1943)
20. Iotsich, ZhRF-KhO, 36, 443 (1904)
21. Klages, Ber., 35, 2633 (1902)
22. Lucas, C.R., 152, 1771 (1911)
23. Stas, Bull. Soc. Belg., 34, 188; C. 125, II, 1268
24. V. M. Tolstopyatov, ZhRF-KhO, 62, 1812 (1930); A. D. Petrov, K. N. Karpov, M. A. Chel'tseva, ZhKh, 6, 522, (1936)
25. Fr. Whitmore, J. Am. Chem. Soc., 64, 2964 (1942)
26. Holler, J. Am. Chem. Soc., 54, 2503 (1932)
27. Young and Roberts, J. Am. Chem. Soc., 66, 1444 (1944)
28. Fr. Whitmore, J. Am. Chem. Soc., 64, 2964 (1942)
29. Kochler, J. Am. Chem. Soc., 54, 4015 (1932); 62, 785 (1940)
30. Young and Roberts, J. Am. Chem. Soc., 66, 2131 (1944)
31. Tarasov, ZhRF-KhO, 41, 1309 (1909)
32. Kus'min, ZhRF-KhO, 41, 1314 (1909)
33. A. Willenart, A. Chem., 107, 12, 345 (1929)
34. A. D. Petrov, V. M. Koptev, E. Kaplan, Izv. AN SSSR, OKhN, 4 (1944)
35. Morton, Chem. Rev., 1, 8 (1944)
36. Kharasch u Weinhouse, J. Org. Chem., 1, 253 (1936)
37. Barnes and Dorevani, Ind. Eng. Chem., 35, 349 (1943)
38. Fr. Whitmore, Wilson, J. Am. Chem. Soc., JACF, 63, 2035 (1941)
39. Miset, C., 1907, I, 1313
40. Young and Roberts, J. Am. Chem. Soc., 67, 1040 (1945)

- END -

- 17 -

~~REDACTED~~